

DE GRUYTER
OPENPol. J. Food Nutr. Sci., 2015, Vol. 65, No. 1, pp. 5–7
<http://journal.pan.olsztyn.pl>

Letter to the Editor

Is There any Relationship Between the Type of Alcoholic Beverage and Oral Cancer? Focus on Red Wine in an European Perspective

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Key words: Mediterranean diet, oral cancer, chemoprevention

Since decades, it has been suggested that regular, low to moderate consumption of red wine, a major component of Mediterranean diet, at main meals, may contribute to explain the healthy properties attributed to this traditional dietary style. Despite preclinical *in vitro/in vivo* data have shown many significant pharmacological activities of grape phytochemicals, mostly polyphenols, evidence in humans is still debated. This lack of consensus may be due to the equilibrium between the two main components of wine relevant for health: alcohol and phytochemicals. Because ethanol is a major risk factor in oral carcinogenesis, in this commentary, we briefly discuss the relationship between the type of alcoholic beverage and oral cancer in European countries.

Even if wine is an alcoholic beverage, a plethora of beneficial biological and pharmacological activities has been ascribed, in the past decades, to some grape and wine metabolites. In particular, polyphenols (Figure 1) possess different molecular and biochemical targets in healthy, altered and damaged cells [Iriti & Vitalini, 2012]. In addition, the diversity of grape and wine chemistry has been recently improved by the discovery of new bioactive molecules in these products, *i.e.* melatonin and phytosterols (Figure 1) [Ruggiero *et al.*, 2013; Vitalini *et al.*, 2013]. Therefore, it can be hypothesized that these and, possibly, other phytochemicals may maximize the healthy properties of polyphenols by additive and/or synergistic effects.

Despite polyphenols are considered the archetype of health benefits attributed to a regular, low to moderate red wine consumption at main meals, as demonstrated in a huge amount of *in vitro/in vivo* experimental models [Iriti & Faoro, 2009], in human evidence it is still inconclusive, possibly because of the presence of ethanol in wine, which may counteract or nullify, to some extent, the protective effects of bioactive phytochemicals in conditions of heavy or binge (episodic heavy) wine intake [Iriti & Varoni, 2013].

The most important risk factors contributing to the etiology of oral cancer, in Western countries, are tobacco smoking and alcohol consumption [Tanaka *et al.*, 2011]. As reported by the International Agency for Research on Cancer [World Health Organization], in 2012, oral cavity cancer ranked as the 12th most common malignancy in Europe (Figure 2). The highest incidence and mortality rates (top 10) of lip, oral cavity and pharynx cancers for both sexes have been recorded in countries distributed in Eastern Europe (Hungary, Slovakia and Romania), Western Europe (France, Germany, Belgium and Switzerland), Northern Europe (Denmark) and Southern Europe (Portugal and Slovenia), according to the geographical sub-regions defined by the United Nations (<http://unstats.un.org>) (Figure 3). Intriguingly, red wine was the most consumed beverage in five out ten countries (Hungary, Portugal, France, Slovenia and Switzerland), beer in four (Romania, Germany, Belgium and Denmark) and spirits in two (Romania and Slovakia) nations (Table 1).

At the end of this brief commentary, our opinion is that preclinical evidences, alone, are not sufficient, and the reported *in vivo/in vitro* pharmacological activities of wine phytochemicals have to be unquestionably confirmed in humans, epidemiological data need to be verified, in order to demonstrate that associations do not arise from casualness, since confounding factors, including lifestyles, may generate a misinterpretation of results.

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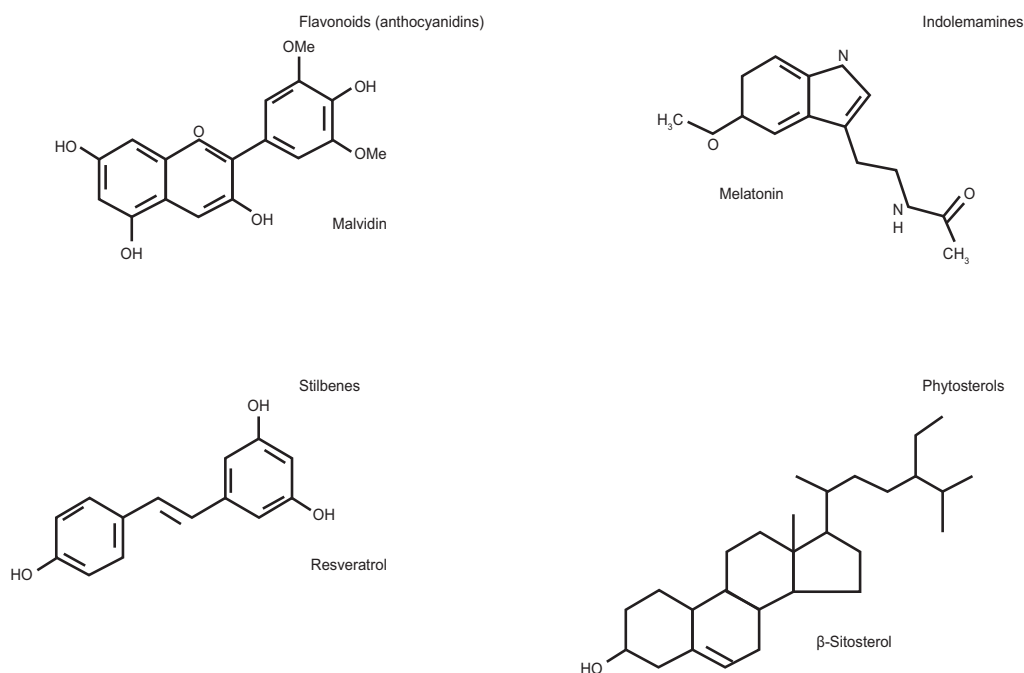


FIGURE 1. Wine chemistry. Wine bioactive phytochemicals include polyphenols (flavonoids and stilbenes), melatonin and phytosterols.

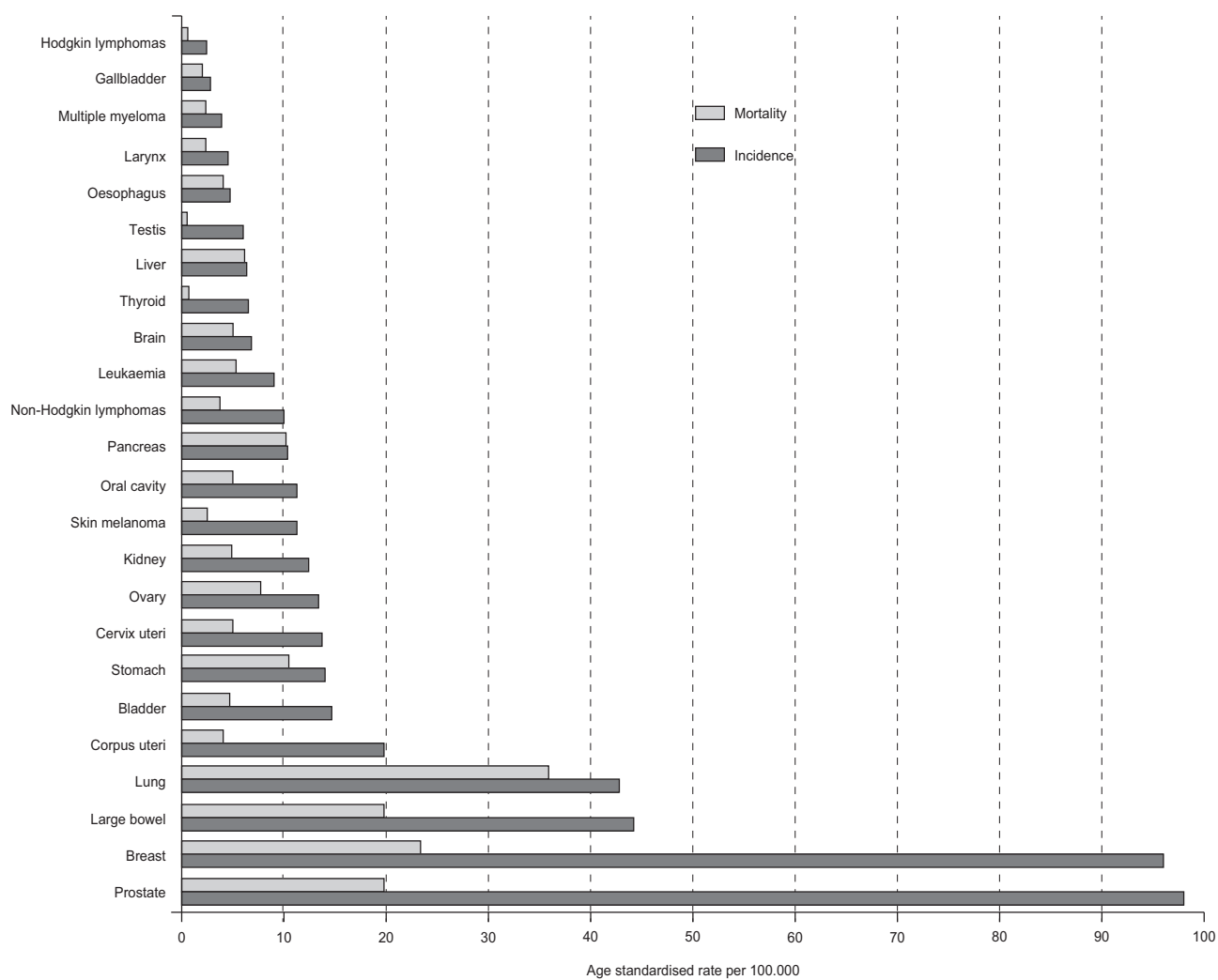


FIGURE 2. Estimated incidence and mortality rates of the most frequent cancers for both sexes in Europe, 2012 (International Agency for Research on Cancer, World Health Organization, <http://eco.iarc.fr/eucan>).

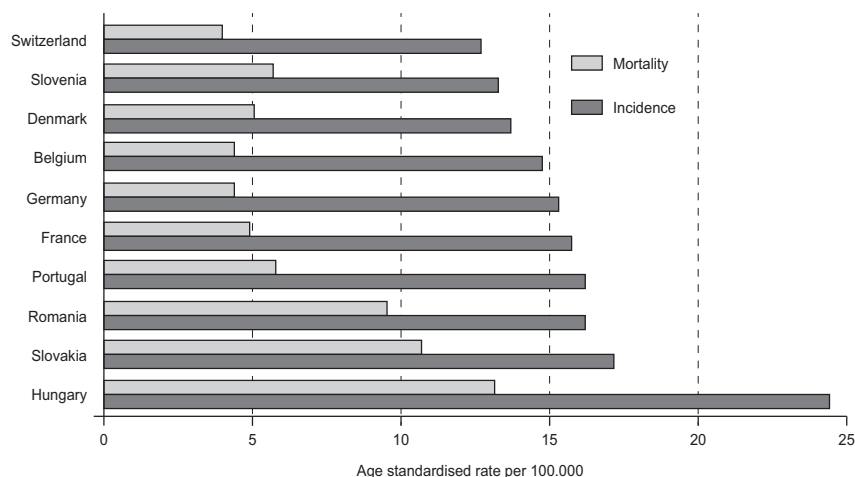


FIGURE 3. Estimated incidence and mortality rates of lip, oral cavity and pharynx cancers for both sexes in Europe (top 10 countries), 2012 (International Agency for Research on Cancer, World Health Organization, <http://eco.iarc.fr/eucan>).

TABLE 1. Recorded adult (15+) alcohol consumption by type of alcoholic beverage (in % of pure alcohol) in selected European countries in 2005* (see Figure 3).

Country	Spirits (%)	Beer (%)	Wine (%)	Other (%)
Hungary	24	35	40	1
Slovakia	49	36	15	0
Romania	39	39	22	0
Portugal	10	31	55	4
France	20	17	62	1
Germany	20	53	27	0
Belgium	6	57	37	< 1
Denmark	16	45	39	0
Slovenia	13	39	48	0
Switzerland	18	31	50	1

*Source: 'European Status Report on Alcohol and Health', WHO (World Health Organization) 2011 (www.euro.who.int).

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Submitted: 17 October 2014. Accepted: 4 November 2014. Published on-line: 9 February 2015.